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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,222	08/07/2001	Wendi V. Rodrigueza	10173-073	3425

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/20/2002 9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/924,222	Rodrigueza
Examiner	**Art Unit**
Gollamudi Kishore	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-16* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Since there are no claims with claim numbers 5-8, claims 9-20 have been renumbered as 5-16. Claims included in the prosecution are 1-16.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear from claim 1 what the patients are treated for. The term, 'large' is a relative term and hence indefinite. The examiner suggests reciting the size ranges.

It is unclear what applicants intend to convey by 'small acceptor of cholesterol' in claim 7. 'Small' is a relative term. Furthermore, the lipoproteins recited in claim 8 are large molecules since they are polymers of amino acids.

'Said small acceptor' in claim 8 lacks an antecedent basis in claim 7 since claim 7 recites 'small acceptor of cholesterol' and not just 'small acceptor. Claim 8 recites 'amphiphilic compound'; the phospholipids which make up the liposomes are amphiphilic. This claim also recites 'small cholesterol acceptor' as a Markush member; this is not further defining the term which is already recited in claim 7 and line 1 of claim 8. 'Small

phospholipid liposomes' is indefinite since the term 'small' is a relative term. Line 7 of claim 8 recites 'said drug including an agent that raises physiologic HDL and the Markush members recited following this expression also recites ' a drug which increases HDL concentrations'. The examiner suggests a thorough revision of this claim and reciting specific compounds.

What is being conveyed by 'phosphatidylcholine mixture thereof in claim 13?

What is being conveyed by 'lipid binding proteins' in claim 15? According to the parent claims, the liposomes are bound to proteins and therefore, those proteins recited in the parent claim are lipid binding proteins.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761

(CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,746,223. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. The claims in the said patent are drawn to a method of forcing the reverse transport of cholesterol from peripheral tissues to the liver which implies the control of hypercholesterolemia which is encompassed by the term, 'dislipidemia' and instant claims are drawn to a method of treating a dislipidemic patient using the same composition. The claims thus, are obvious varients.

5. Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S.

Patent No. 6,312,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. The claims in the said patent are drawn to a method of treatment of atherosclerosis using the same claimed composition. Atherosclerosis is a result of cholesterol deposition in the blood vessels due to impaired cholesterol metabolism (hypercholesterolemia : a lipid condition) and therefore, the treated patient is a dislipidemic patient is implicit. The term, 'dislipidemia' encompasses 'hypercholesterolemia' and instant claims are drawn to a method of treating a dislipidemic patient using the same composition. The claims thus, are obvious variants.

Claim Rejections - 35 U.S.C. § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2, 4-9 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 470 437 of record.

EP teaches unilamellar liposomes having an average diameter of 100 nm containing phosphatidylcholine for the treatment of atherosclerosis and increased fat values (note page 7; also columns 5-7 of its English Equivalent, US. Instant claims recite 'a method of

treating a dislipidemic patient'. Since atherosclerosis is the result of cholesterol deposition, the patient being a dislipidemic patient is implicit.

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

8. Claims 1-9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP cited above.

EP does not provide specific examples for the treatment of atherosclerosis and increased fat values. It would however, been obvious to an artisan to use liposomes for the treatment of atherosclerosis based on the teachings of EP. EP does not specifically state that the phosphatidylcholine used should be from eggs. EP does not also specifically teach instant protocol of administration. In the absence of showing unexpected results, these parameters are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

9. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (BBA, 875, pp., 183-194, 1986) by itself or in combination with EP cited above.

Williams teaches a method of administration of liposomes and liposomes together with plasma (contains lipoproteins) and the alterations in lipid metabolism and the regression of experimental atherosclerosis as a result of such an administration (note the Materials and Methods section and the discussion). What is lacking in Williams is the teachings of the sizes of liposomes. However, the methodology disclosed on pages 184 and 185 indicated that sonicated liposomes were passed through a 0.22 microns filter and therefore, it would have been obvious to one of ordinary skill in the art that the liposomes would contain liposomes of instant sizes. Even assuming that the sizes in Williams are different from instant sizes, one of ordinary skill in the art would be motivated to use liposomes larger than 50 nm with a reasonable expectation of success since EP which deals with the treatment of same disease state advocates the use of liposomes of instant sizes.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP or Williams cited above, further in view of Allen (J. Liposome Research, 1992).

EP, and Williams do not teach the attachment of molecules such as PEG to the liposomes. The use of these molecules in the liposome preparations of EP would have been obvious to one of ordinary skill in the art since Allen teaches that the attachment of PEG to liposomes increases their stability and circulation times (note the abstract).

The references are all of record.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is

more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

September 19, 2002